CLAIMS

What is claimed as the invention is:

1. An oncolytic virus having a genome in which a promoter polynucleotide is operably linked to a genetic element essential for replication or assembly of the virus, wherein the promoter polynucleotide preferentially promotes transcription of the genetic element in cells expressing telomerase reverse transcriptase (TERT), thereby promoting replication of the virus, and wherein replication of the virus in a cancer cell leads to lysis of the cancer cell.

2. The oncolytic virus of claim 1, which is a replication-conditional adenovirus.

3. The oncolytic adenovirus of claim 2, wherein the genetic element essential for replication is an adenovirus E1a region.

4. The oncolytic virus of any of claims 1-3, further comprising an encoding region whose expression is toxic to the cell, or which renders the cell more susceptible to toxic effects of a drug.

5. The oncolytic virus of claim 4, wherein the encoding region encodes thymidine kinase, and the drug is ganciclovir.

6. The oncolytic virus of any preceding claim, wherein the promoter polynucleotide is a promoter for TERT.

7. The oncolytic virus of any preceding claim, wherein the promoter polynucleotide is a human telomerase reverse transcriptase (hTERT) promoter or a mouse telomerase reverse transcriptase (mTERT) promoter.

8. The oncolytic virus of any preceding claim, wherein the promoter polynucleotide comprises a c-Myc binding site.

9. The oncolytic virus of any preceding claim, wherein the promoter polynucleotide has one or more of the following features:

a) it comprises the sequence from position –117 to position –36 relative to the translation initiation site (position 13545) of SEQ. ID NO:1;

b) it comprises the sequence from position –239 to position –36 relative to the translation initiation site (position 13545) of SEQ. ID NO:1;

c) it comprises the sequence from position –117 to position +1 relative to the translation initiation site (position 13545) of SEQ. ID NO:1;

d) it comprises the sequence from position –239 to position +1 relative to the translation initiation site (position 13545) of SEQ. ID NO:1; or

c) it hybridizes with a polynucleotide complementary to a sequence having feature a), b), c), or d) under stringent conditions, and has the characteristic of preferentially promoting transcription in cells expressing TERT.

10. The oncolytic virus of any preceding claim, wherein the promoter has one or more of the following features:

a) it comprises a sequence of at least about 100 consecutive nucleotides in SEQ. ID NO:1;

b) it comprises a sequence of at least about 500 consecutive nucleotides in SEQ. ID NO:1;

c) it comprises a sequence of at least about 100 consecutive nucleotides in SEQ. ID NO:2;

d) it comprises a sequence of at least about 500 consecutive nucleotides in SEQ. ID NO:2; or

e) it hybridizes with a polynucleotide complementary to a sequence having feature a), b), c) or d) under stringent conditions, and has the characteristic of preferentially promoting transcription in cells expressing TERT.

11. A recombinant polynucleotide in which a promoter is operatively linked to an encoding region, wherein the encoding region is preferentially transcribed in cells expressing TERT, and wherein the promoter has one or more of the following features:

a) it comprises the sequence from position –117 to position –36 relative to the translation initiation site (position 13545) of SEQ. ID NO:1;

b) it comprises the sequence from position –239 to position –36 relative to the translation initiation site (position 13545) of SEQ. ID NO:1;

c) it comprises the sequence from position –117 to position +1 relative to the translation initiation site (position 13545) of SEQ. ID NO:1;

d) it comprises the sequence from position –239 to position +1 relative to the translation initiation site (position 13545) of SEQ. ID NO:1; or

c) it hybridizes with a polynucleotide complementary to a sequence having feature a), b), c), or d) under stringent conditions.

12. A recombinant polynucleotide in which a promoter is operatively linked to an encoding region, wherein the encoding region is preferentially transcribed in cells expressing TERT, and wherein the promoter consists of no more than 82 consecutive nucleotides.

13. An isolated polynucleotide having one or more of the following features:

a) it comprises a sequence of at least about 100 consecutive nucleotides in SEQ. ID NO:1;

b) it comprises a sequence of at least about 500 consecutive nucleotides in SEQ. ID NO:1; or

c) it hybridizes with a polynucleotide complementary to a sequence having feature a), b), c) or d) under stringent conditions, and has the characteristic of preferentially promoting transcription in cells expressing TERT; wherein said polynucleotide is not entirely contained in SEQ. ID NO:6 of PCT Application WO98/14593.

14. The isolated polynucleotide of claim 11 further comprising a heterologous encoding region, wherein the encoding region is preferentially transcribed in cells expressing TERT.

15. A method for selecting a virus having characteristics of an oncolytic virus according to any of claims 1-10, comprising providing a recombinant virus in which a promoter polynucleotide is operably linked to a genetic element required for replication of the virus, using the virus to infect a cell expressing TERT and a cell not expressing TERT, and selecting the virus if it preferentially kills the cell expressing TERT.

16. A method of regulating transcription of an encoding region operatively linked to a promoter, wherein the promoter preferentially promotes transcription of the encoding region in cells expressing TERT, and the method comprises modulating a transcriptional regulatory element within the promoter.

17. The method of regulating transcription according to claim 16, wherein the transcriptional regulatory element is modulated by a factor selected from the group consisting of c-Myc, SP1, SRY, HNF-3ß, HNF-5, TFIID-MBP, E2F and c-Myb.

18. The method of regulating transcription according to claim 17, wherein the factor is c-Myc.

19. The method of regulating transcription according to claim 18, wherein c-Myc is modulated by contacting the cell with a ligand for the estrogen receptor.

20. The method of regulating transcription according to any of claims 16-19, wherein the encoding region encodes TERT.

21. The method of regulating transcription according to any of claims 16-19, wherein the encoding region is heterologous to the promoter.

22. A method for expressing a polynucleotide in a cell, comprising transducing the cell with a vector in which the polynucleotide is operably linked to an hTERT promoter comprising an E box, and then treating the cell to increase binding of a transcriptional regulatory factor to the E box.

23. A method of treating a subject for a disease associated with increased expression of TERT in affected cells, comprising administering to the subject an effective amount of the oncolytic virus according to any of claims 1-10.

24. The method of claim 23, wherein the disease is a cancer.

25. Use of the oncolytic virus according to any of claims 1-10 in the preparation of a medicament for treatment of a human or animal body.

26. Use of the oncolytic virus according to any of claims 1-10 in the preparation of a medicament for treatment of cancer.

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